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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/961,201	09/24/2001	Vishva M. Dixit	PF335D2	6537

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HUMAN GENOME SCIENCES INC
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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/961,201	DIXIT ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,12,14,15 and 17-74* is/are pending in the application.

4a) Of the above claim(s) *1,10,12,14,15,17-20,33,34 and 54-56* is/are withdrawn from consideration.

5)☐ Claim(s) *21-26, and 30-31* is/are allowed.

6)☒ Claim(s) *27-29,32,35-53,and 57-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1, 10, 12, 14-15, and 17-74 are pending.

2. Applicant's election with traverse of Group IV, Claim 13 (now claims 21-32, 35-53, and 57-74) drawn to antibody and hybridoma, filed 8/4/03, is acknowledged. The traversal is on the grounds that (1) Groups I-X represented distinct or independent inventions, restriction remains improper unless it can be shown that the search and examination of all groups would entail a "serious burden"; (2) a search of the polypeptide claims would also provide useful information for the claims of the other groups. These arguments are not found persuasive for the following reasons. The inventions of Groups I-X have acquired a separate status in the art because of their recognized divergent subject matter for the reason set forth in the restriction requirement mailed 7/2/03. Furthermore, the fields of search for each of the inventions are different and not coextensive. Thus, a search of all inventions of Groups I-X poses an undue burden on the Examiner. With regard to the newly added claims 21-74, it is noted that claims 21-32, 35-53, and 57-74 (Group IV), drawn to an isolated antibody, classified in Class 530, subclass 387.1, while Claims 33-34 and 54-56 (Group XI) drawn to a method of detecting ICD-LAP 6 protein using antibody, classified in Class 435, subclass 7.1. Inventions of Group III and Group XI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the antibody as claimed can be used in materially different process such as treating immune disease. Therefore, they are patentably distinct. The requirement of Group IV and Groups (I-III, V-XI) is still deemed proper and is therefore made FINAL.

3. Claims 1, 10, 12, 14-15, 17-20, 33-34 and 54-56 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 21-32, 35-53, and 57-74 are being acted upon in this Office Action.

5. Applicant is advised that should claim 44 be found allowable, claim 47 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 42-53, and 57-63 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the polypeptide encoded by the cDNA contained in ATCC Deposit number 1095150 is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the cDNA contained in ATCC Deposit, which produces this antibody, may satisfy first paragraph. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which case the statement need not be verified. See MPEP 1.804 (b).

8. Claims 68-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for an isolated antibody or fragment thereof that specifically binds to a protein as set forth in claims 21-53, and 57-67 for detection assays (page 18), **does not** reasonably provide enablement for (1) *any* isolated antibody or fragment thereof obtained from an animal that has been immunized with any protein "**comprising**" an amino acid sequence such as the amino acid sequence of amino acid residues 10 to 20, 40 to 50, 70 to 90 or 100 to 113 of SEQ ID NO: 1 wherein said antibody or fragment thereof specifically binds to said amino acid sequence, (2) the antibody or fragment thereof obtained from an animal that has been immunized with any protein "**comprising**" an amino acid sequence such as the amino acid sequence of amino acid residues 10 to 20 of SEQ ID NO: 1, (3) the antibody or fragment thereof obtained from an animal that has been immunized with any protein "comprising" an amino acid sequence such as the amino acid sequence of amino acid residues 40 to 50 of SEQ ID NO: 1, (4) the antibody or fragment thereof obtained from an animal that has been immunized with any protein "comprising" an amino acid sequence such as the amino acid sequence of amino acid residues 70 to 90 of SEQ ID NO: 1, (5) the antibody or fragment thereof obtained from an animal that has been immunized with any protein "comprising" an amino acid sequence such as the amino acid sequence of amino acid residues 100 to 113 of SEQ ID NO: 1, and (6) the isolated antibody or fragment thereof obtained from an animal that has been immunized with any protein "comprising" an amino acid sequence such as the amino acid sequence of amino acid residues 10 to 20, 40 to 50, 70 to 90 or 100 to 113 of SEQ ID NO: 1 which is a monoclonal antibody, a chimeric antibody, a polyclonal antibody, a humanized antibody, a single chain antibody or an Fab fragment for detection assays. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a polypeptide of interleukin-1 beta converting enzyme like apoptosis protease 6 (ICE-LAP6) of SEQ ID NO: 1 encoded by cDNAs contained in ATCC Deposit Number 1095150 (page 22). The specification further discloses antibodies such as polyclonal, monoclonal, chimeric, single chain, and humanized antibodies as well as antibody fragment thereof such as Fab fragments that binds specifically to polypeptides of interleukin-1 beta converting enzyme like apoptosis protease 5 (ICE-LAP6) of SEQ ID NO: encoded by cDNAs contained in ATCC Deposit Number 1095150, respectively for detection assays (page 45-46).

The specification does not provide *any* guidance as how to make and use *any* isolated antibody or fragment thereof obtained from an animal that has been immunized with *any* protein an amino acid sequence such as the amino acid sequence of amino acid residues 10 to 20, 40 to 50, 70 to 90 or 100 to 113 of SEQ ID NO: 1 because the term "comprising" is open-ended. It expands the amino acid residues mentioned above to include additional amino acids at either or both ends. There is insufficient guidance as to what types of amino acid residues to be added and whether the resulting antibody generated from immunizing an mammal with the undisclosed protein would bind specifically to the amino acid sequence of amino acid residues 10 to 20, 40 to 50, 70 to 90 or 100 to 113 of SEQ ID NO: 1. There are no working examples demonstrating the binding specificity of any antibody such as monoclonal, chimeric, polyclonal, humanized, single chain and Fab fragment thereof that bind specifically to the amino acid sequence such as amino acid residues 10 to 20, 40 to 50, 70 to 90 or 100 to 113 of SEQ ID NO: 1.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Furthermore, it is well known in the art at the time the invention was made that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular).

Kuby *et al* teach that immunizing a peptide versus a full-length polypeptide may result in **antibody specificity** that differs from antibody specificity directed against the native full-length polypeptide.

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the indefinite number of undisclosed "protein", it is unpredictable which undisclosed protein would generate antibody that binds specifically to amino acid residues 10 to 20, 40 to 50, 70 to 90 or 100 to 113 of SEQ ID NO: 1, in turn, would be useful for any purpose.

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

9. Claims 68-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* isolated antibody or fragment thereof obtained from an animal that has been immunized with any protein "**comprising**" an amino acid sequence such as the amino acid sequence of amino acid residues 10 to 20, 40 to 50, 70 to 90 or 100 to 113 of SEQ ID NO: 1 wherein said antibody or fragment thereof specifically binds to said amino acid sequence, (2) the antibody or fragment thereof obtained from an animal that has been immunized with any protein "**comprising**" an amino acid sequence such as the amino acid sequence of amino acid residues 10 to 20 of SEQ ID NO: 1, (3) the antibody or fragment thereof obtained from an animal that has been immunized with any protein "comprising" an amino acid sequence such as the amino acid sequence of amino acid residues 40 to 50 of SEQ ID NO: 1, (4) the antibody or fragment thereof obtained from an animal that has been immunized with any protein "comprising" an amino acid sequence such as the amino acid sequence of amino acid residues 70 to 90 of SEQ ID NO: 1, (5) the antibody or fragment thereof obtained from an animal that has been immunized with any protein "comprising" an amino acid sequence such as the amino acid sequence of amino acid residues 100 to 113 of SEQ ID NO: 1, and (6) the isolated antibody or fragment thereof obtained from an

animal that has been immunized with any protein "comprising" an amino acid sequence such as the amino acid sequence of amino acid residues 10 to 20, 40 to 50, 70 to 90 or 100 to 113 of SEQ ID NO: 1 which is a monoclonal antibody, a chimeric antibody, a polyclonal antibody, a humanized antibody, a single chain antibody or an Fab fragment for detection assays.

The specification discloses only a polypeptide of interleukin-1 beta converting enzyme like apoptosis protease 6 (ICE-LAP6) of SEQ ID NO: 1 encoded by cDNAs contained in ATCC Deposit Number 1095150 (page 22). The specification further discloses antibodies such as polyclonal, monoclonal, chimeric, single chain, and humanized antibodies as well as antibody fragment thereof such as Fab fragments that binds specifically to polypeptides of interleukin-1 beta converting enzyme like apoptosis protease 5 (ICE-LAP6) of SEQ ID NO: encoded by cDNAs contained in ATCC Deposit Number 1095150, respectively for detection assays (page 45-46).

Other than the specific antibody or fragment thereof obtained from an animal that has been immunized with the specific protein mentioned above, there is inadequate written description about the structure associated with functions of any protein "comprising" an amino acid sequence of amino acid residues such as 10 to 20, 40 to 50, 70 to 90 or 100 to 113 of SEQ ID NO: 1 because the term "comprising" is open-ended. It expands the amino acid residues mentioned above to include additional amino acids at either or both ends. There is inadequate written description about the undisclosed amino acid residues to be added, much less about the binding specificity of the claimed antibody. With regard to *any* isolated antibody such as polyclonal, monoclonal, chimeric, humanized, single chain and Fab fragment thereof that binds to any protein consisting of any portion of SEQ ID NO: 1 wherein said portion consists of at least 30 or 50 contiguous amino acid sequence of SEQ ID NO: 1 or polypeptide encoded by the cDNA contained in ATCC deposited Number 1095150, there is inadequate written description about the binding specificity of the claimed antibody, much less to which portion of SEQ ID NO: 1 or the polypeptide encoded by the cDNA contained in ATCC deposited Number 1095150 that the claimed antibody binds. Since the protein for immunizing the animal is not adequately described and/or the binding specificity of the antibody is not adequately described, the antibody such as monoclonal, chemeric, polyclonal, humanized, single chain and fragment thereof obtained from animal immunized with the undisclosed protein is not adequately described.

Further, the specification discloses only antibodies that bind to interleukin-1 beta converting enzyme like apoptosis protease 6 (ICE-LAP6) of SEQ ID NO: 1 encoded by cDNAs

contained in ATCC Deposit Number 1095150.. Given the lack of a written description of *any* additional representative species of protein for immunizing an animal for making the claimed antibody, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. Claims 68-74 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

The "amino acid residues **10 to 20** of SEQ ID NO: 1, ...amino acid residues **40 to 50** of SEQ ID NO: 1...amino acid residues **70 to 90** of SEQ ID NO: 1, ...amino acid residues **100 to 113** of SEQ ID NO: 1 " in Claim 68 represents a departure from the specification and the claims as originally filed. The passages pointed out by applicant in the amendment filed 8/4/03 do not provide a clear support for the said specific amino acid residues.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

12. Claims 27-29, 32, 35-41, 48-50, 53, 57-62, and 64-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "fragment thereof" which is a human antibody in claims 27, 48, and 66 is ambiguous and indefinite because only antibody can be a human antibody and not antibody fragment can be a human antibody. One of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

The "fragment thereof" which is a polyclonal antibody in claims 28, and 49 is ambiguous and indefinite because only antibody can be a polyclonal antibody and not antibody fragment can

be a polyclonal antibody. One of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

The "fragment thereof" which is a monoclonal antibody in claims 29, 40, 50, 62, 65 and 73 is ambiguous and indefinite because only antibody can be a monoclonal antibody and not antibody fragment can be a monoclonal antibody. One of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

The "fragment thereof" in claims 32 and 53 is indefinite and ambiguous because hybridoma does not produce antibody fragment. One of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

The "fragment thereof" in claims 35-39, 57-61, and 68-72 is indefinite and ambiguous because only antibody, not antibody fragment, can be obtained from animal that has been immunized with a protein.

The antibody that binds to ICE-LAP 6 protein in claim 64 "is encoded by a polynucleotide encoding amino acids 1 to 416 of SEQ ID NO: 1 operably associated with a regulatory sequence that controls the expression of said polynucleotide is ambiguous and indefinite because if the antibody or fragment thereof binds to a protein consisting of 1 to 416 of SEQ ID NO: 1, then the claim should recite that protein.

13. Claims 21-26, and 30-31 are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist (customer service) whose telephone number is (703) 872-9305.

15. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401. The IFW official Fax number is (703) 872-9306. For After Final, the Fax number is (703) 872-9307.

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